THE ROLE OF THE RENAL NERVES IN THE ANTINATRIURESIS ASSOCIATED WITH ACUTE THORACIC INFERIOR VENA CAVA CONSTRICTION IN THE DOG

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INTRODUCTION AND REVIEW OF THE LITERATURE

Constricting the thoracic inferior vena cava in the dog is a potent stimulus for renal sodium retention (Davis, Howell and Southworth, 1953) but the mechanism(s) mediating this response remain obscure. Based on studies by several groups of investigators it is evident that sodium retention in this model cannot be adequately explained by a decrease in glomerular filtration rate and renal blood flow or an increase in renal venous pressure or aldosterone secretion.

Davis and colleagues (Davis, Howell and Southworth, 1953; Davis, Holman, Carpenter, Urquhart and Higgins, 1964) found that sodium retention did not correlate with changes in glomerular filtration rate or renal plasma flow whereas Levinsky and Lalone (1965) demonstrated that the antidiuretic influence of caval constriction could not be reversed by infusing large volumes of saline that augmented glomerular filtration rate.

An elevation in renal venous pressure has also been excluded as a necessary factor by the observation that constricting the abdominal inferior vena cava sufficiently to raise renal venous pressure to levels produced by constricting the thoracic inferior vena cava does not promote sodium retention (Levinsky and Lalone, 1965; Cirksena, Dirks and Berliner, 1966) and that transplanting the kidney to the neck, a maneuver that prevents an increase in renal venous

pressure, does not eliminate the antinatriuretic response to caval constriction (Carpenter, Davis, Holman, Ayers and Bahn, 1961; Davis, Holman, Carpenter, Urquhart and Higgins, 1964).

Although aldosterone levels are elevated in this animal model (Davis, Kliman, Yankopoulos and Peterson, 1958), hyperaldosteronism is not essential since sodium retention was observed in adrenalectomized animals given either minimal mineralocorticosteroid replacement (Davis, Howell and Southworth, 1953) or high sodium diet without hormone replacement (Davis, Howell, Goodkind and Hyatt, 1956).

Several lines of evidence suggest that the sympathetic nervous system may play an important role in mediating renal sodium retention under various conditions. For example Barger, Muldowney and Liebowitz (1959) postulated that increased renal nerve stimulation is an important factor in the antinatriuresis observed in dogs with experimental congestive heart failure. These investigators infused Dibenzyline, an alpha adrenergic blocking agent, into the renal artery of dogs with tricuspid insufficiency and pulmonary stenosis and observed a significant increase in sodium excretion from the ipsilateral kidney whereas no effect was seen when Dibenzyline was infused into the renal artery of normal dogs. That the sympathetic nervous system may participate in the normal regulation of sodium balance was suggested by Gill and Bartter (1966) who reported that sympathetic blockade induced with guanethidine diminished the capacity of the kidney

of normal man to conserve sodium in response to sodium deriva-tion. More recently Gill and Casper (1969) have shown that renal sodium retention in response to hemorrhage can be mediated by increased renal nerve stimulation that is not sufficient to decrease glomerular filtration rate.

Evidence which suggests increased sympathetic activity may participate in the renal sodium retention of caval constriction was first obtained by Whelan, McCoord and Schilling (1952) who noted that the kidney transplanted to the neck failed to exhibit the same degree of sodium retention as the intact kidney in response to caval constriction. Additional support derives from the study of Gill, Carr, Fleischmann, Casper and Bartter (1967). These investigators produced autonomic blockade with pentolinium in dogs with caval constriction and observed a significant increase in sodium excretion which suggests a heightened level of autonomic activity was present in these animals.

Although these data implicate a role for the sympathetic nervous system in mediating the antinatriuresis associated with caval constriction, Davis, Holman, Carpenter, Urquhart and Higgins (1964) concluded that the renal nerves were not essential for renal sodium retention to occur. These investigators performed bilateral adrenalectomy and unilateral nephrectomy and transplanted the remaining kidney to the neck which effectively denervated the kidney. Nevertheless, these animals still retained sodium and developed

ascites in response to caval constriction. Thus these experiments exclude an essential role for the renal nerves in the response, but as Gill, Carr, Fleischmann, Casper and Bartter (1967) have stated, they do not exclude the possibility that an increase in circulating catecholamines derived from a systemic increase in sympathetic stimulation may have existed in these animals. Thus in view of the heightened sensitivity of the denervated kidney to circulating norepinephrine (Berne, Hoffman, Kagan and Levy, 1952), the net result might mimic the response produced by renal nerve stimulation. Moreover it should be emphasized that these studies were performed in chronic animals and therefore do not exclude a role for the renal nerves in the antinatriuretic response to acute caval constriction.

Thus far there have been no studies which define the contribution of the renal nerves in modulating the renal handling of sodium during acute caval constriction. To answer this question the effect of acute caval constriction on sodium excretion was examined in dogs with and without intact renal nerves.

MATERIALS AND METHODS

All studies were performed in female mongrel dogs weighing 13 to 31 kg fed a standard kennel ration. In some animals, seven to fourteen days prior to the study, an inflatable cuff constrictor was placed around the thoracic portion of the inferior vena cava through a right thoracic incision and a button for inflating the cuff was brought out through a small skin incision. On the day prior to the study the animal was deprived of food but water was permitted ad libitum. On the morning of the study the animal was anesthetized with ether sodium pentobarbital or sodium pentothal, 25 mg/kg, administered intravenously with supplemental doses as required to maintain light anesthesia. An endotracheal tube was inserted and the animal was ventilated with a Harvard respiratory adjusted to maintain the arterial pH between 7.35 and 7.45. Polyethylene catheters were inserted in a femoral artery, femoral vein, and both jugular veins to permit sampling of bloods, monitoring of pressures, and infusing solutions. A foley catheter was placed in the urinary bladder.

All animals received a priming dose of inulin and p-amino hippurate (PAH) followed by a constant infusion of these substances in 0.9% saline at 2.0 ml/min. Aqueous Pitressin was added to the infusion in an amount calculated to deliver 0.5 mU/kg/min. A minimum of sixty minutes was allowed for equilibration of solutions before collecting urine

samples. Approximately two hours prior to collecting urine samples the animal was given desoxycorticosterone acetate (DOCA), 10 mg, intramuscularly.

Experimental protocol: Group I consisted of 11 experiments. After collecting three consecutive 10 minute control urine samples, 0.9% saline was infused at 0.5 ml/min/kg for 60 minutes into a femoral vein following which three consecutive 10 minute experimental urine samples were collected.

Group II consisted of 8 experiments. After collecting three control urine samples as in group I, saline was infused at 0.5 ml/min/kg for 60 minutes while simultaneously the thoracic inferior vena cava was constricted by inflating the cuff. After 60 minutes had elapsed three 10 minute experimental urine samples were collected. The degree of constriction was designed to produce a slight fall in renal perfusion pressure which was usually associated with a moderate reduction in cardiac output but not glomerular filtration rate. Those studies in which glomerular filtration rate fell by more than ten per cent were excluded.

Group III consisted of 8 animals in which acute renal denervation was performed on the morning of the study. After exposing the kidney through a left subcostal flank incision, the renal artery was stripped of all visible nerve fibers then coated with phenol. A 20 gauge needle attached to a polyethylene catheter was inserted in the renal vein through the ovarian vein to permit sampling of renal vein blood.

Because it was not possible to assess whether renal innervation to the right kidney had been altered during the surgical procedure, urine was collected only from the left kidney via a catheter inserted in the left ureter. To exclude the possibility of denervation natriuresis influencing the results, a minimum of 120 minutes elapsed from the time of denervation before steady state control urine samples were collected. A steady state was assumed to exist if three consecutive 10 minute urine volumes varied by less than 10 per cent. The remainder of the protocol was identical to that of group II.

Data Collection: Aortic and inferior vena cava pressures were continuously monitored with Statham pressure transducers, models 23 AA, from catheters inserted in a femoral artery and vein. Cardiac output was determined at approximately the midpoint of each 10 minute period using a dye dilution technique. Indocyanine green, 2.5 mg, was injected through a catheter secured in the jugular vein and arterial blood was withdrawn from a femoral arterial catheter through a Gilford densitometer cuvette using a Harvard constant withdrawal syringe pump. Cardiac output was calculated according to the method of Kinsman, Moore and Hamilton (1929).

Arterial blood was collected at the midpoint of each period. In group III renal venous blood was collected simultaneously in chilled test tubes and centrifuged immediately to permit separation of the plasma within 5 minutes of the time of collection.

Urine and blood samples were analyzed for sodium using an Instrumentation Laboratories flamephotometer. Inulin was determined by the method of Schreiner (1950) and PAH by the method of Smith, Finkelstein, Aliminosa, Crawford and Graber (1945). Plasma proteins were measured using the biuret reaction and packed cell volume was measured using a micro-hematocrit centrifuge.

Calculations: Absolute sodium excretion in μEq/min was determined from the formula $U_{Na}V$ where U_{Na} equals urine sodium concentration in μEq/ml and V equals urine flow in ml/min. Fractional sodium excretion (FE_{Na}) in % was calculated as $U_{Na}V/F_{Na}$ where F_{Na} equals filtered sodium and was determined by the product of plasma sodium concentration (P_{Na}) in μEq/ml and glomerular filtration rate (GFR) in ml/min. GFR was estimated from the clearance of inulin (C_{IN}) according to the formula $C_{IN} = U_{IN}V/P_{IN}$ where U_{IN} equals urine concentration of inulin and P_{IN} equals th plasma concentration of inulin. In groups I and II renal cortical plasma flow was estimated from the clearance of PAH (C_{PAH}) calculated according to the formula $C_{PAH} = U_{PAH}V/P_{PAH}$ where U_{PAH} and P_{PAH} equal the urine and plasma concentrations of PAH respectively. In group III renal blood flow was calculated from the extraction of PAH according to the formula RBF = RPF/(1-0.95 PCV). RPF equals renal plasma flow and was calculated according to the formula $RPF = U_{PAH}V/(A_{PAH}-V_{PAH})$ where A_{PAH} and V_{PAH} equal the arterial and renal venous plasm

concentrations of PAH respectively. Filtration fraction (FF) was calculated from the formula $FF = C_{IN}/RPF$. Renal perfusion pressure (PP_R) was calculated from the formula $PP_R = P_A - P_V$ where P_A and P_V equal mean aortic and mean inferior vena cava pressures respectively. Cardiac index was calculated as CI = CO/kg body weight where CO equals cardiac output. Systemic vascular resistance (SVR) was calculated according to the formula $SVR = (P_A - P_V)/CI$ expressed in PRU per kg body weight where PRU equals peripheral resistance units in mmHg/ml/min.

Statistical evaluation of data: Student's t-test was used to evaluate paired data within each group and mean data between the groups.

RESULTS

The data in the text and figures are presented as the mean $\pm$ SEM. The control period represents the mean of three 10 minute periods prior to and the experimental period the mean of three minute periods after caval constriction and/or saline infusion.

Group I - renal response to saline infusion: Table 1 summarizes the data from individual experiments. Infusing saline at 0.5 ml/kg for 60 minutes resulted in a significant increase in $U_{NA}V$ from 222.6 $\pm$ 58.9 to 572.4 $\pm$ 117.2 μEq/min, $p < 0.005$. Fractional sodium excretion (FE_{Na}) increased from

2.0 ± 0.5 to 5.0 ± 1.1 %, $p < 0.005$. The increase in sodium excretion could not be related to alterations in glomerular filtration rate which changed in a variable manner in individual experiments but without a significant change in the mean for the group. C_{IN} measured 80.2 ± 5.0 ml/min during control and 79.7 ± 6.4 ml/min during saline infusion. In contrast renal cortical plasma flow, estimated from C_{PAH}, decreased in 9 of 11 experiments with a significant decrease occurring in the mean for the group. C_{PAH} measured 260 ± 23 ml/min during control and 222 ± 18 ml/min during saline infusion, $p < 0.025$. Renal perfusion pressure (PP_R) increased in 10 of 11 experiments and the mean PP_R increased from 114 ± 7 mmHg during control to 141 ± 6 mmHg during saline infusion. Cardiac index (CI), however, changed in a variable manner in individual experiments but there was no significant change in the mean for the group. CI measured 178 ± 24 ml/min per kg during control and 175 ± 21 ml/min per kg during the experimental period.

Group II - influence of acute constriction of the thoracic inferior vena cava on the renal response to saline loading in dogs with intact renal nerves: Table 2 summarizes the data from individual experiments. The mean $U_{Na}V$, FE_{Na}, C_{IN}, C_{PAH}, PP_R, CI and plasma protein concentration during the control period in Group II were not different statistically from the control values of the same variables in group I. When the inferior vena cava was constricted during the

infusion of saline, sodium excretion decreased in contrast with the increase seen in group I. $U_{Na}V$ decreased from a control value of 276.0 ± 59.9 to 132.2 ± 29.1 μEq/min, $p < 0.05$, and FE_{Na} decreased from 2.5 ± 0.4 to 1.3 ± 0.4 %, $p < 0.025$. C_{IN} changed in a variable manner in individual experiments with no apparent relation between the change in C_{IN} and the magnitude of the fall in $U_{Na}V$. Mean C_{IN} did not change measuring 76.0 ± 8.6 ml/min during control and 75.9 ± 7.7 ml/min during the experimental period whereas C_{PAH} fell from 315 ± 34 to 210 ± 23 ml/min, $p < 0.01$. In contrast with group I PP_R tended to decrease in most studies although the mean decrease in PP_R from 116 ± 6 to 107 ± 4 mmHg was not significant, $p > 0.1$. CI, however, decreased in 7 animals with a significant decrease in the mean for the group. Control CI measured 185 ± 14 ml/min per kg and fell to 131 ± 10 ml/min per kg during caval constriction, $p < 0.001$. Figure 1 contrasts the mean responses of the group I and group II experiments.

Group III - influence of acute constriction of the thoracic inferior vena cava on the renal response to saline loading in dogs with renal denervation. Table 3 summarizes the data from individual experiments. In group III the renal function data were obtained from one kidney only which explains the lower control $U_{Na}V$ and C_{IN} compared with groups I and II. In contrast with the response seen in group II, caval constriction during saline loading did not produce an

antinatriuresis in the denervated kidney in group III. Rather a significant increase in sodium excretion occurred. $U_{Na}V$ increased from 165.2 ± 47.5 to 247.2 ± 36.2 μEq/min, $p < 0.025$, and FE_{Na} increased from 2.0 ± 0.3 to 3.2 ± 0.3 %, $p < 0.025$. The natriuresis was not related to changes in C_{IN} which were variable but with no change in the mean for the group. Mean C_{IN} was 52.9 ± 6.6 ml/min during control and 52.6 ± 6.5 ml/min during the experimental period. RBF measured by the extraction of PAH decreased in all experiments with the mean RBF decreasing from 302 ± 41 ml/min during the control period to 226 ± 32 ml/min during the experimental period, $p < 0.01$. Control PP_R averaged 132 ± 5 mmHg and decreased to 115 ± 6 mmHg during caval constriction. The fall in PP_R was associated with a significant decrease in CI from 176 ± 25 ml/min per kg during control to 125 ± 15 ml/min per kg during caval constriction.

Figure 2 compares group II and group III with respect to FE_{Na}, C_{IN}, PP_R, CI and systemic vascular resistance (SVR). C_{IN} in group II was factored by 2 to approximate function in a single kidney and then it was normalized in both groups by dividing through by body weight. There was no significant difference between control FE_{Na} in group II and III, $p > 0.3$, whereas during the experimental period FE_{Na} in group III was significantly higher than in group II, $p < 0.01$. There was no significant differences in C_{IN} when normalized as described above. Control C_{IN} measured 2.1 ± 0.2 ml/min per kg body

weight in group II and 2.2 ± 0.2 ml/min per kg in group III, $p > 0.5$, and did not change in either group during caval constriction. Control PP_R in group III was slightly greater than that in group II, $0.1 > p > 0.05$, but there was no difference in PP_R during the experimental period, $p > 0.2$. CI was the same in both groups during the control period, $p > 0.8$, and fell to the same extent during caval constriction, $p > 0.6$. SVR was slightly higher in group III measuring 0.874 ± 0.138 and 1.039 ± 0.159 PRU per kg body weight during the control and experimental periods respectively compared to 0.672 ± 0.098 and 0.833 ± 0.084 PRU per kg body weight during the control and experimental periods in group II. However, these differences were not statistically significant, $p > 0.05$ for the control and $p > 0.2$ for the experimental periods. The increase in SVR within each group, however, was significant, $p < 0.01$.

DISCUSSION

The present experiments were designed to evaluate the role of the renal nerves in mediating the antinatriuresis of acute constriction of the thoracic inferior vena cava. The results provide strong evidence to support the conclusion that the renal nerves constitute the major efferent pathway through which acute caval constriction stimulates renal sodium retention.

In group I the infusion of saline caused a significant increase in sodium excretion whereas in group II caval constriction not only prevented the natriuretic response to saline it caused a significant decrease in sodium excretion that was unrelated to changes in glomerular filtration rate. In contrast when the kidney was denervated in group III, caval constriction did not cause an antinatriuresis so that the natriuretic stimulus of saline infusion became evident.

The conclusion that the difference between the response in group II and group III was related to renal denervation in group III is valid providing the two groups were similar in other respects. First it is possible that renal denervation altered baseline renal function which resulted in a delayed natriuresis. For example it is well known that acute renal denervation may cause a denervation natriuresis (Marshall and Kolls, 1919; Kriss, Futcher and Goldman, 1948; Kamm and Levinsky, 1965; Bonjour, Churchill, and Malvin, 1969). However, this possibility was excluded by delaying urine collections for at least 120 minutes from the time of renal denervation and waiting until a steady state urine flow was established. In addition, the fact that control FE_{Na} and control C_{IN} corrected for body weight were the same in both groups (see Figure 2), suggests that renal denervation did not significantly alter baseline renal function in group III. Second, it is unlikely that the natriuresis in group III reflected an inadequate degree of caval constriction which

resulted in a weak antinatriuretic stimulus since, as shown in figure 2, the change in cardiac index, systemic vascular resistance and renal perfusion pressure were similar in the two groups suggesting that the inferior vena cava was constricted to a similar degree in both groups. Third it is unlikely that the natriuresis in group III reflected a greater degree of volume expansion resulting in a more potent natriuretic stimulus that exceeded the antinatriuretic stimulus of caval constriction since a uniform rate of saline infusion adjusted for body weight was used in all experiments. Moreover, plasma protein concentration decreased to the same extent in both groups indicating a similar degree of plasma expansion had occurred. Therefore since the two groups were similar with respect to those identifiable variables which might influence sodium excretion, it is concluded that denervating the kidney interrupted the efferent pathway through which acute constriction of the thoracic inferior vena cava stimulates renal sodium retention.

The present experiments support and extend the observations of Whelan, McCoord and Schilling (1952) that the transplanted (denervated) kidney is less responsive to caval constriction than the intact kidney, and the observations of Gill, Carr, Fleischmann, Casper and Bartter (1967) that ganglionic blockade increases sodium excretion in dogs with caval constriction. In addition, these findings support the broader concept of Gill and Casper (1969) that the sympathetic nervous

system may constitute a final common pathway for the renal conservation of sodium when the effective intravascular volume is decreased from whatever cause. These authors demonstrated that the renal sodium retention observed in response to hemorrhage is mediated through the renal nerves. Similarly an increase in renal sympathetic tone was also postulated to be the mechanism responsible for sodium retention in dogs with experimentally induced heart failure (Barger, Muldowney and Liebowitz, 1959; Barger, Yates and Rudolph, 1961). Activation of the sympathetic nervous system in the present experiments occurred presumably in response to the fall in cardiac output and perfusion pressure. That the fall in cardiac output and not hepatic congestion was the important stimulus that activated the antinatriuretic response is supported by the observations of Schreier, Humphreys, Ufferman and Earley (1971) that constriction of the thoracic superior vena cava produced changes in sodium excretion and systemic hemodynamics entirely similar to those seen with constriction of the inferior vena cava. However, these studies do not exclude the possibility that hepatic congestion, particularly of a chronic nature, may participate in the afferent or efferent limb of the antinatriuretic response.

Although the present experiments support a major role for the renal nerves in the antinatriuresis of acute caval constriction, other factors are probably involved. Since the natriuresis in group III was of lesser magnitude than that in

group I, it suggests that renal denervation did not interrupt entirely the antinatriuretic stimulus of caval constriction. In part this may reflect incomplete renal denervation which could explain the decrease in RBF in group III. In addition, the decrease in renal perfusion pressure may have altered the renal handling of sodium (Friedler, Belleau, Martins and Earley, 1967; Earley and Friedler, 1966). Finally the experiments of Davis, Holman, Carpenter, Urquhart and Higgins (1964) in which sodium retention and ascites developed in adrenalectomized dogs with a solitary kidney transplanted in the neck also implicate some other factor in the antinatriuresis of caval constriction. It has been suggested that an increase in circulating catecholamines released in response to generalized sympathetic stimulation might explain the above findings. Alternatively it is possible that some other humoral factor with antinatriuretic activity mediated the response. However, if such a factor does exist, the present experiments suggest that it does not play a major role in the antinatriuresis of acute caval constriction.

The mechanism whereby an increase in renal nerve stimulation leads to a decrease in sodium excretion has not been clearly established. Barger and colleagues have postulated that sympathetic stimulation effects a redistribution of renal blood that promotes sodium retention. In dogs with experimentally induced heart failure, a redistribution of blood flow from the superficial cortex to the inner cortex can be

demonstrated (Barger, 1966). A similar redistribution is seen during hemorrhage (Carriere, Thorburn, O'Morchoe, and Barger, 1966) and in response to mild renal nerve stimulation (Pomeranz, Birtch and Barger, 1968). In contrast the diuretic agents furosemide and ethacrynic acid have an opposite effect, i.e. cortical blood flow is increased and juxtamedullary blood flow is decreased (Birtch, Zakheim, Jones and Barger, 1967). These observations suggest that increasing blood flow and filtrate to the superficial cortical nephrons promotes a natriuresis whereas redistributing blood flow and filtrate to the juxtamedullary nephrons promotes sodium retention. That such a mechanism may be operating in dogs with caval constriction receives support from the work of Cannon and Kilcoyne (1969) who report finding a similar redistribution of renal blood flow from superficial to medullary nephrons in caval dogs.

In addition to redistribution of renal blood flow, antinatriuresis might also have occurred as a consequence of an increase in renal vascular resistance and fall in peritubular capillary pressure as suggested by Friedler, Belleau, Martino and Earley (1967). If the fall in C_{PAH} in group II mirrored a fall in renal blood flow, then the data from group II suggest that renal vascular resistance increased, presumably at the efferent arteriole since GFR did not change and could have promoted increased tubular sodium transport.

The data do not permit any definite conclusion concerning how the renal nerves effected a decrease in sodium excretion. It is of interest that renal denervation in group III resulted in a natriuresis despite a decrease in renal blood flow and perfusion pressure and an increase in renal vascular resistance and filtration fraction. Thus it is conceivable that the renal nerves may alter sodium transport by a mechanism unrelated to changes in intrarenal hemodynamics.

LITERATURE CITED

Barger, A. C. 1966. Renal hemodynamic factors in congestive heart failure. Ann. N. Y. Acad. Sci. 139:276-284.

Barger, A. C., Muldowney, F. P., and Liebowitz, M. R. 1959. Role of the kidney in the pathogenesis of congestive heart failure. Circulation 20:273-285.

Barger, A. C., Yates, F. E., and Rudolph, A. M. 1961. Renal hemodynamics and sodium excretion in dogs with graded valvular damage and in congestive heart failure. Am. J. Physiol. 200:601-608.

Berne, R. M., Hoffman, W. K. Jr., Kagan, A., and Levy, M. N. 1952. Response of the normal and denervated kidney to l'epinenephrine and l'norepinephrine. Am. J. Physiol. 171:564-571.

Birtch, A. G., Zakheim, R. M., Jones, L. G., and Barger, A. C. 1967. Redistribution of renal blood flow produced by furosemide and ethacrynic acid. Circ. Res. 21:869-878.

Bonjour, J., Churchill, P. C., and Malvin, R. L. 1969. Change of tubular reabsorption of sodium and water after renal denervation in the dog. J. Physiol. 204:571-582.

Cannon, P. J., and Kilcoyne, M. D. 1969. Alterations in intrarenal blood flow distribution during acute partial occlusion of the thoracic inferior vena cava. Clin. Res. 17:426.

Carpenter, C. C. J., Davis, J. O., Holman, J. E., Ayers, C. R., and Bahn, R. C. 1961. Studies on the response of the transplanted kidney and the transplanted adrenal gland to thoracic inferior vena caval constriction. J. Clin. Invest. 40:196-204.

Carriere, S., Thorburn, G. D., O'Morchoe, C. C. C., and Barger, A. C. 1966. Intrarenal distribution of blood flow in dogs during hemorrhagic hypotension. Circ. Res. 19:167-179.

Cirksena, W. J., Dirks, J. H., and Berliner, R. W. 1966. Effect of thoracic cava obstruction on response of proximal tubule sodium reabsorption to saline infusion. J. Clin. Invest. 45:179-186.

Davis, J. O., Holman, J. E., Carpenter, C. C. J., Urquhart, J. and Higgins, J. T. Jr. 1964. An extra-adrenal factor essential for chronic renal sodium retention in presence of increased sodium-retaining hormone. Circ. Res. 14:17-31.

Davis, J. O., and Howell, D. S. 1953. Mechanisms of fluid and electrolyte retention in experimental preparations in dogs. II. With thoracic inferior vena cava constriction. Circ. Res. 1:171-178.

Davis, J. O., Howell, D. S., Goodkind, M. J., and Hyatt, R. E. 1956. Accumulation of ascites during maintenance of adrenalectomized dogs with thoracic inferior vena cava constriction on a high socium diet without hormone therapy. Am. J. Physiol. 185:230-234.

Davis, J. O., Howell, D. S., and Southworth, J. L. 1953. Mechanisms of fluid and electrolyte retention in experimental preparations in dogs. III. Effect of adrenalectomy and subsequent desoxycorticosterone acetate administration on ascites formation. Circ. Res. 1:260-270.

Davis, J. O., Kliman, B., Yankopoulos, N. A., and Peterson, R. E. 1958. Increased aldosterone secretion following acute constriction of the inferior vena cava. J. Clin. Invest. 37:1783-1790.

Earley, L. E., and Friedler, R. M. 1966. The effects of combined renal vasodilatation and pressor agents on renal hemodynamics and the tubular reabsorption of sodium. J. Clin. Invest. 45:542-551.

Friedler, R. M., Belleau, L. J., Martino, J. A., and Earley, L. E. 1967. Hemodynamically induced natriuresis in the presence of sodium retention resulting from constriction of the thoracic inferior vena cava. J. Lab. Clin. Med. 69:565-583.

Gill, J. R. Jr., and Bartter, F. C. 1966. Adrenergic nervous system in sodium metabolism. II. Effects of Guanethidine on the renal response to sodium deprivation in normal man. N. Engl. J. Med. 275:1466-1470.

Gill, J. R. Jr., Carr, A. A., Fleischmann, L. E., Casper, A. G. T., and Bartter, F. C. 1967. Effects of pentolinium on sodium excretion in dogs with constriction of the vena cava. Am. J. Physiol. 212:191-196.

Gill, J. R. Jr., and Casper, G. T. 1969. Role of the sympathetic nervous system in the renal response to hemorrhage. J. Clin. Invest. 48:915-922.

Kamm, D. E., and Levinsky, N. G. 1965. The mechanism of denervation natriuresis. J. Clin. Invest. 44:93-102.

Kinsman, J. M., Moore, J. W., and Hamilton, W. F. 1929. Studies on the circulation. I. Injection method: Physical and mathematical considerations. Am. J. Physiol. 89:322-330.

Kriss, J. P., Futcher, P. H., and Goldman, M. L. 1948. Unilateral adrenalectomy, unilateral splanchnic nerve resection and homolateral renal function. Am. J. Physiol. 154:229-240.

Levinsky, N. G., and Lalone, R. C. 1965. Sodium excretion during acute saline loading in dogs with vena caval constriction. J. Clin. Invest. 44:565-573.

Marshall, E. K. Jr., and Kolls, A. C. 1919. Studies on the nervous control of the kidney in relation to diuresis and urinary secretion. Am. J. Physiol. 49:302-316.

Pomeranz, B. H., Birtch, A. G., and Barger, A. C. 1968. Neural Control of intrarenal blood flow. Am. J. Physiol. 215:1067-1081.

Schreier, R. W., Humphreys, M. H., Ufferman, R. C., and Earley, L. E. 1971. Afferent and efferent mechanisms involved in the antinatriuretic effect of acute constriction of the thoracic vena cava. Clin. Res. 19:154.

Schreiner, G. E. 1950. Determination of Inulin by means of resorcinol. Proc. Soc. Exptl. Biol. Med. 74:117-120.

Smith, H. W., Finklestein, N., Aliminosa, L., Crawford, B., and Graber, M. 1945. The renal clearances of substituted hippuric acid derivatives and other aromatic acids in dogs and man. J. Clin. Invest. 24:388-404.

Whelan, T. J., McCoord, A. B., and Schilling, J. A. 1952. Experimental ascites: The influence of transplantation of the kidneys to the neck. Surgical Forum 4:510-516.

APPENDIX

Table 1. Response to saline infusion in group I.*

Exp. No.	$U_{Na}V$ µEq/min		FE_{Na} %		C_{IN} ml/min		C_{PAH} ml/min		PP_R mmHg		CI ml/min/kg		Plasma Protein g/100 ml		Weight kg
	C	E	C	E	C	E	C	E	C	E	C	E	C	E	
1	15.4	92.0	0.2	1.1	62.9	56.9	205	152	104	146	162	127	4.6	3.8	17.5
2	31.1	272.5	0.3	2.8	74.1	67.6	213	176	84	148	175	189	4.4	3.6	15.3
3	124.3	583.5	0.9	3.4	103.1	120.8	322	282	122	128	136	116	6.0	5.0	22.2
4	346.4	717.8	3.1	6.2	74.6	73.7	266	193	115	161	165	148	5.7	4.6	20.5
5	288.3	387.6	2.5	2.6	86.3	94.9	175	198	166	162	105	109	5.2	4.2	19.4
6	158.7	994.0	1.6	7.1	85.6	98.1	267	252	122	141	110	156	5.7	3.9	30.0
7	166.5	364.6	1.0	3.0	102.1	84.0	295	281	98	121	153	170	5.5	4.9	21.0
8	117.4	305.8	1.1	2.8	76.4	75.2	342	203	98	148	152	113	5.3	3.9	15.2
9	723.5	1386.2	5.3	9.8	94.4	95.4	334	273	142	171	397	346	5.6	4.5	16.4
10	268.5	890.8	4.0	12.5	48.1	49.9	116	131	95	109	232	264	4.6	3.3	13.8
11	208.6	301.7	1.9	3.2	74.3	60.2	328	301	110	115	170	183	4.2	4.3	19.6

Footnote to Table 1

* $U_{Na}V$ = absolute sodium excretion, FE_{Na} = fractional sodium excretion, C_{IN} = inulin clearance, C_{PAH} = PAH clearance, PP_R = renal perfusion pressure, CI = cardiac index, C = control period, E = experimental period.

Table 2. Effect of caval constriction on response to saline infusion in group II*

Exp. No.	$U_{Na}V$ µEq/min		FE_{Na} %		C_{IN} ml/min		C_{PAH} ml/min		PP_R mmHg		CI ml/min/kg		Plasma Protein g/100 ml		Weight kg
	C	E	C	E	C	E	C	E	C	E	C	E	C	E	
2	40.5	10.6	0.6	0.1	46.5	48.4	208	136	116	84	201	104	5.3	3.7	15.6
3	225.6	94.4	2.1	0.8	75.1	79.5	316	216	133	111	216	133	4.9	3.0	19.0
4	308.1	197.2	2.1	1.3	113.0	114.7	449	247	103	103	203	131			22.0
5	586.7	87.4	4.3	0.7	95.7	88.7	329	193	115	113	178	183	5.9	4.7	18.0
16	214.7	177.5	3.5	3.2	43.0	47.0	442	337	118	109	152	120	4.6	4.0	15.8
17	165.5	50.3	1.9	0.5	61.4	68.8	177	143	105	104	235	141	4.3	3.8	13.8
18	226.8	201.7	1.9	1.8	84.6	81.8	320	172	92	107	184	146	5.9	4.8	15.8
19	440.2	238.7	3.5	2.1	88.3	78.0	279	239	144	123	110	88	6.1	4.3	24.2
MEAN	276.0	132.2	2.5	1.3	76.0	75.9	315	210	116	107	185	131	5.3	4.0	18.0
±SEM	59.9	29.1	0.4	0.4	8.6	7.7	34	23	6	4	14	10	0.3	0.2	1.3
P	<0.05		<0.025		NS		<0.01		NS		<0.001		<0.001		

* $U_{Na}V$ = absolute sodium excretion, FE_{Na} = fractional sodium excretion, C_{IN} = inulin clearance, C_{PAH} = PAH clearance, PP_R = renal perfusion pressure, CI = cardiac index, C = control period, E = experimental period.

Table 3. Effect of caval constriction on the response to saline infusion in group III with renal denervation*

Exp. No.	$U_{Na}V$ µEq/min		FE_{Na} %		C_{IN} ml/min		RBF ml/min		RVR PRU		PP_R mmHg	
	C	E	C	E	C	E	C	E	C	E	C	E
20	234.5	315.3	2.2	2.9	78.9	78.6	467	392	0.25	0.27	115	106
21	66.3	104.9	1.2	2.0	36.8	34.9	192	152	0.68	0.81	131	123
22	74.7	200.4	1.6	4.0	32.9	33.7	219	168	0.59	0.69	130	116
23	130.0	167.8	2.1	2.8	42.5	40.3	281	203	0.48	0.59	135	120
24	115.4	301.7	2.0	4.6	40.2	44.6	168	151	0.92	0.91	155	138
25	155.4	276.1	1.7	3.0	61.7	62.6	468	324	0.24	0.26	114	83
26	468.2	427.2	4.2	3.8	79.8	78.4	299	168	0.47	0.80	142	135
27	77.0	184.3	1.1	2.7	50.3	47.5	321	247	0.40	0.41	130	101
MEAN	165.2	247.2	2.0	3.2	52.9	52.6	302	226	0.51	0.59	132	115
±SEM	47.5	36.2	0.3	0.3	6.6	6.5	41	32	0.08	0.09	5	6
P	<0.025		<0.025		NS		<0.01		0.1>p>0.05		<0.01	

* $U_{Na}V$ = absolute sodium excretion, FE_{Na} = fractional sodium excretion, C_{IN} = inulin clearance, RBF = renal blood flow, RVR = renal vascular resistance, PP_R = renal perfusion pressure, CI = cardiac index, PCV = packed cell volume, FF = filtration fraction, C = control period, E = experimental period.

Table 3. (continued)

Exp. No.	CI		PCV		FF		Plasma Protein		Weight
	ml/min/kg		%				g/100 ml		kg
	C	E	C	E	C	E	C	E	
20	307	195	33	34	0.23	0.29	5.0	4.1	23.8
21	102	79	41	37	0.31	0.35	5.1	4.0	21.4
22	184	154	39	32	0.24	0.29	5.6	4.0	20.5
23	129	97	48	35	0.28	0.29	5.4	4.2	23.0
24	101	78	44	38	0.41	0.46	5.5	4.2	24.5
25	204	148	44	43	0.23	0.32	5.8	4.5	21.2
26	225	144	34	30	0.40	0.65	5.2	4.3	31.0
27	152	106	51	43	0.30	0.33	6.0	3.9	22.8
MEAN	176	125	42	37	0.30	0.37	5.4	4.2	23.5
±SEM	25	15	2	2	0.03	0.04	0.1	0.1	1.2
P	<0.01		<0.025		<0.05		<0.001		

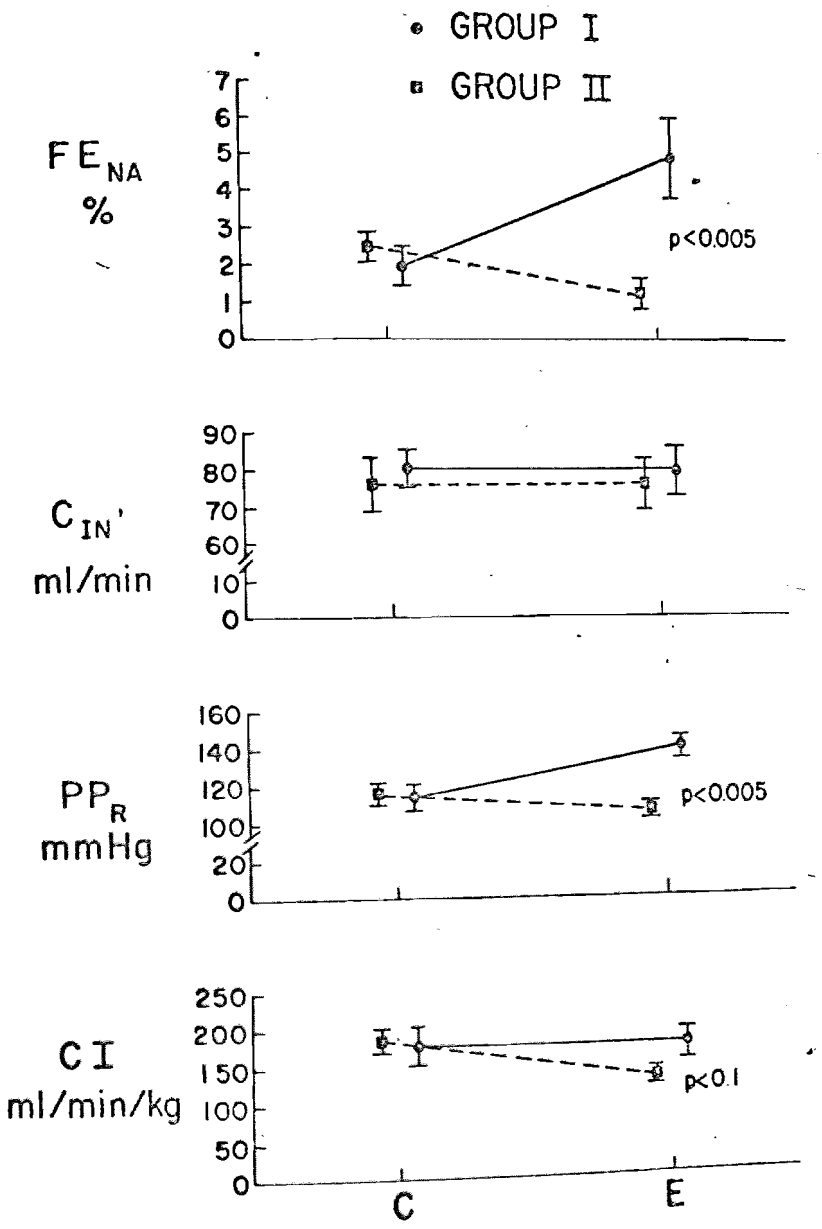

Figure 1. Comparison of renal function and systemic hemodynamics in Groups I and II. FE_{Na} = fractional sodium excretion, C_{IN} = inulin clearance, PP_R = renal perfusion pressure, CI = cardiac index.

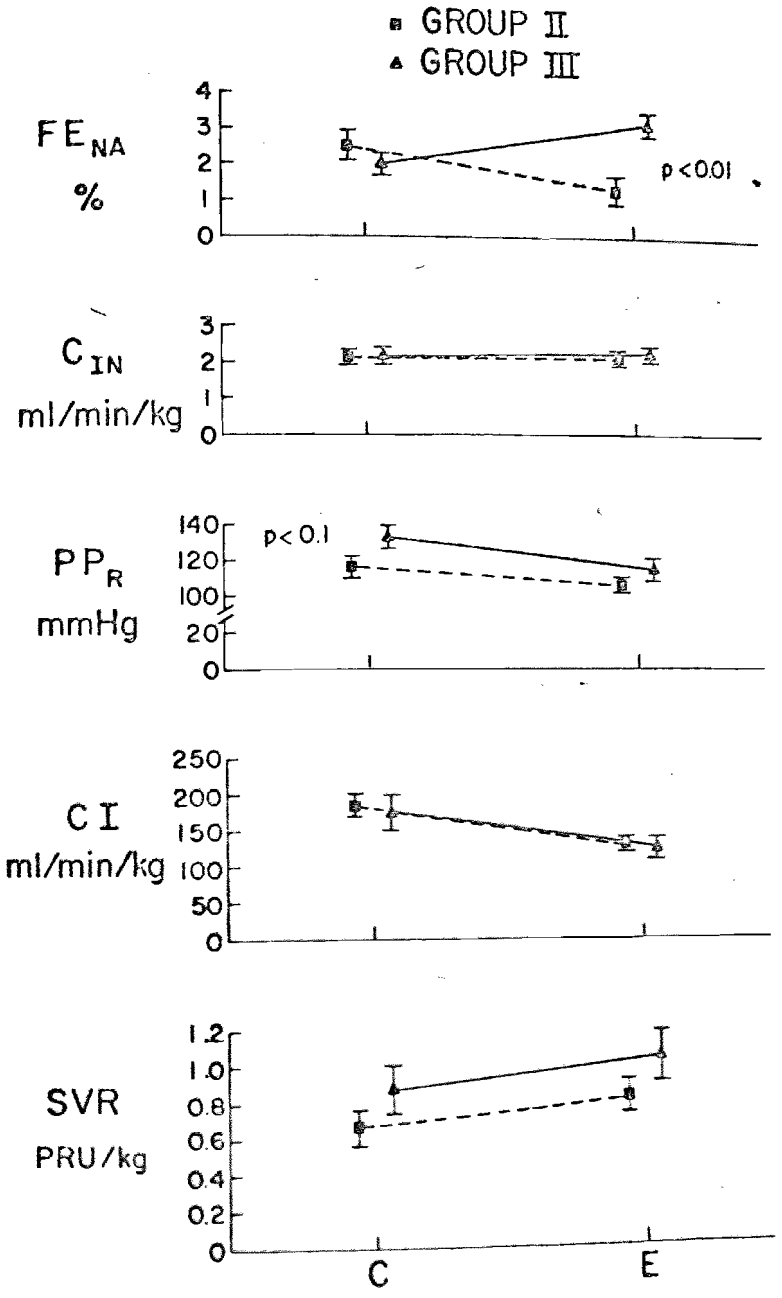

Figure 2. Comparison of renal function and systemic hemodynamics in Groups II and III. FE_{Na} = fractional sodium excretion, C_{IN} = inulin clearance, PP_R = renal perfusion pressure, CI = cardiac index, SVR = systemic vascular resistance.